Notice of Allowability	Application No.	Applicant(s)	
	10/070,279	MARTIN, THOMAS	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *21 January 2005*.

2. ☒ The allowed claim(s) is/are *11-22*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 21Jan05
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____.
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Response to Amendment

As requested in the correspondence from applicant filed 21 January 2005, which is in reply to the Office action mailed 2 September 2004 (hereinafter "previous Office action"), claims 11-22 have been amended, and the abstract amended.

Status of Claim Rejections - 35 USC § 112

In the previous Office action, claims 15, 16, 21 and 22, drawn to methods of treatment, were rejected under the first paragraph of this statute, for lack of an enabling disclosure.

In view of the amendments to those claims, the rejection is hereby withdrawn. It is noted that although applicant disagrees with the finding of lack of enablement of the full scope of all of the (previously) claimed methods, these claims have been further limited in scope.

The finding of lack of enablement set forth in the previous Office action alleged that *no* disease was treatable with compounds according to invention, which compounds are inhibitors of tryptases, without an undue amount of experimentation on the part of whomever wished to do so. In making the enablement rejection, the examiner relied on two references, authored by Wright et al and Burgess, to show what was known about the potential therapeutic application of tryptase inhibitors at the time the invention was made.

In response, applicant has presented two references, authored by Krishna et al and Rice et al, respectively, which show that for one of ordinary skill to treat a disease selected from asthma, allergic conjunctivitis, allergic rhinitis, psoriasis, sclerodermatitis

and inflammatory bowel disease (to which claims 15, 16, 21 and 22 are now limited), it would not require an undue amount of experimentation.

The position held by the examiner, that the instantly claimed methods are not enabled for any disease, has been tempered by these two new references, cited by applicant.

The two references provided do not directly contradict the conclusion reached by the aforementioned Wright et al reference, which alleged that although a tryptase inhibitor had shown some effectiveness in attenuating antigen-induced airway hyperresponsiveness in animals, it remained to be seen whether inhibition of tryptases would indeed prove to be a viable treatment option for asthma. Instead, Krishna et al and Rice et al serve to show that the body of knowledge, at the time the invention was made, concerning therapeutic application of tryptase inhibitors was more well-developed than one might think from considering the Wright et al and Burgess references alone.

Methods of treatment according to claims 15, 16, 21 and 22 are not required to be *extremely effective* methods of treatment, all that is required under the law is *some* level of treatment in order for the claim to have been enabled. Wright et al's concern was that tryptase inhibitors might not prove to the best treatment ever for asthma. In light of the newly cited references brought to the attention of the examiner by applicant, it is conceded that asthma is treatable with a tryptase inhibitor sans an undue amount of experimentation.

Also in the previous Office action, a reference authored by Burgess was cited by the examiner to show the state of the art. This reference teaches that *in vitro* activity shown by tryptase inhibitors is not a good predictor of *in vivo* activity of the same. Burgess does, however, suggested that these types of drugs held promise in the treatment of many diseases, such as asthma, psoriasis, allergic conjunctivitis and allergic rhinitis (page 148).

Rice et al, provided by applicants, shows that a tryptase inhibitor had in fact advanced to phase II clinical trials for ulcerative colitis and psoriasis by 2000. This demonstrates that the examiner's position, specifically, that treatment of some of the diseases recited in the instantly claimed methods might not be possible at all, was incorrect.

The fact that asthma, particularly allergen-induced asthma, has been treated with tryptase inhibitors, and that this is reported in both references cited by the examiner (Wright et al and Burgess), and also the two newly cited references by applicant (Krishna et al and Rice et al), would suggest that treatment asthma and related allergic responses, like allergic conjunctivitis and allergic rhinitis, is possible without an undue amount of experimentation.

Page 1044 of Krishna et al suggests that a tryptase inhibitor may be useful in the treatment of scleroderma. Rice et al, as mentioned in the preceding paragraphs, reports that a tryptase inhibitor was (in 2000) in clinical trials for psoriasis. Psoriasis is a skin disease mediated by immunological processes, and much evidence pointing to the potential for tryptase inhibitors in treatment of allergic rhinitis and allergic conjunctivitis

was known at the time the invention was made. In light of these facts, treatment of sclerodermatitis, also an allergic-type condition (inflammation and thickening of the skin), would not require an undue amount of experimentation.

Thus, the rejection of claims 15, 16, 21 and 22 under 35 U.S.C. 112, first paragraph, is hereby withdrawn.

Also in the previous Office action, claims 11-22 were rejected under the first paragraph of 35 U.S.C. 112, for lack of enablement of the full scope of all solvates of the compounds according to the claims.

It is noted that applicant has traversed the rejection, but has deleted "solvates" from the claims, to advance prosecution.

Accordingly the rejection of claims 11-22 on the grounds that solvates, generally, of the compounds are not enabled by the disclosure, is hereby withdrawn.

Specification

In the previous Office action, the abstract was objected to because although structural variables, M, B1, B2, B3 *etc.* were referred to, no generic structure showing these elements' spatial relationship to one another was shown.

Applicant's submission of a revised abstract has obviated this objection.

Allowable Subject Matter

Claims 11-22 are allowed.

The following is an examiner's statement of reasons for allowance:

All previously stated claim rejections have been overcome by argument and amendments.

The closest prior art with respect to the compounds according to claims 11 and 17 (the independent claims in the application) was the basis for rejections under 35 U.S.C. 102 in the non-final rejection mailed 26 April 2004.

Instantly claimed compounds are novel and unobvious for the parts of the molecule linking the K1 and K2 moeities to the central "M" core, which is a dibutynyl element.

The references cited in the rejections under 35 U.S.C. 102 (Office action mailed 26 April 2004), authored by Crisp et al and Rødbotten et al, are the only references disclosing compounds bearing a close similarity to the unusual compounds according to the instant claims.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

All Post-Allowance Correspondence concerning this application must be mailed to:

Mail Stop Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Or you can fax them to the Office of Patent Publications at 703-872-9306, in order to expedite the handling of such correspondence as amendments under 37 CFR 1.312; information disclosure statements, and formal drawings. Sending Post-Allowance

papers to Technology Center 1600 will only cause delays in matching papers with the case.

For information concerning status of correspondence sent after receipt of the Notice of Allowance, please contact the Correspondence Branch at (703) 305-8027. The Notice of Allowance also has an insert containing contact information on other items, including Issue Fees, receipt of formal drawings and the status of the application.

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RICHARD L. RAYMOND
PRIMARY EXAMINER
ART UNIT 1624